Metal Dependent Repressor 1 (Mdr1): DNA Complex

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Abstract No. berk8197
Beamline(s): **X12C**

Archae have been studied for over twenty years as an independent domain of life separate from bacteria and eucarya. They live in a highly diverse range of conditions including thermophilic temperatures or high salt areas. Despite being prokaryotic and having morphology similar to bacteria, genomic sequencing and biochemical studies have shown that the transcription machinery in Archea is more similar to the eucaryal RNA Polymerase II than to the bacterial polymerase machinery. Additionally, archae homologs of TBP and TFIIB have been found and studied biochemically and structurally.

Although the basal transcription machinery has been well studied, very little is known presently regarding the regulation of transcription. Analysis of Archae has failed to identify any evidence for the presence of homologs to the TBP Associated Factors (TAFs), mediator, or any other eucaryal coactivator or corepressor. Instead, several sequences have been found that are homologous to bacterial transcriptional regulators. Our collaborator has recently identified Mdr1 and shown that it regulates transcription on the MDR1 operon in a metal dependent manner. Mdr1 is homologous to the bacterial metal dependent repressor, DtxR. Mdr1 was shown to bind to the operator and repress transcription by preventing the recruitment of RNA Polymerase to the promoter.

We have purified and crystallized the MDr1:DNA complex. A search for freezing conditions is presently underway. Two promising PEG crystal conditions are being pursued. We hope to solve the structures of Mdr1 alone and bound to DNA in order to best appreciate how this archael repressor prevents transcription in vivo.